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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,868	05/04/2001	Wei-Qiang Gao	GENENT.035C1	1085

7590 07/19/2006

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EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,868	GAO, WEI-QIANG	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/14/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-17 and 19-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14-17, and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-12,14-17 and 19-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647. The Examiner for this Application is now Daniel C. Gamett.

2. The amendments of 06/14/2004 have been entered in full. Claims 1-12, 14-17, and 19-21 are under examination.

3. All prior objection/rejections not specifically maintained in this office action are hereby withdrawn.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

5. Upon further consideration, previous indications of allowability are hereby withdrawn.

Claim Rejections - 35 USC § 112

6. Claim 1-8, 10, 12, 14-17 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The fact that a patent is directed to method entailing use of a compound, rather than to the compound *per se*, does not remove patentee's obligation to provide description of the compound sufficient to distinguish infringing methods from noninfringing methods (University of Rochester v.

G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004)). In this case, the claims are drawn to methods that require variants and fragments of heregulin molecules. With regard to "variants", claims 1, 3-8, 10, 14, and 16 recite no limitations as to how much variability is permitted. Claims 2, 15, and 17 recite 126 amino acid residue positions in HRG-α that may be substituted (by any amino acid), deleted, or replaced by insertion. The substitutions alone indicate 20^{125} unique combinations. 20^{36} substitution variants of HRG-β are recited in claims 19-21. As for 'fragments", the claims do not indicate what portions of the recited sequences must be preserved in any fragment; indeed a single amino acid from heregulin might be regarded as a fragment encompassed by the claims. Thus, the genus of claimed heregulin polypeptides is very large. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the claim recites the function of activating HER2 and/or HER3 receptors but then permits practically unlimited deviation from reference sequences. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

7. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written

description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). With the exception of the specifically recited reference sequences, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

8. Therefore, only methods utilizing isolated polypeptides comprising specifically recited amino acid sequences but not the full breadth of the claim meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

9. Claims 1, 3-8, 10, 12, 14, and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6017886 (Carnahan), which claims priority from August 5, 1998. As noted on the record (Office Action 12/06/2002; Applicant's remarks 03/06/2003), Carnahan discloses methods for treating vestibular disorders such as loss of balance due to utricular degeneration or disease in mammals, including humans, by administering effective amounts of NDF/heregulin hybrid peptide composed of both alpha and beta forms. Carnahan also disclose a method for treating hearing loss in mammals, including humans, which is attributable to the degeneration of inner ear hair cells. The heregulin peptide acts by regenerating the inner ear hair cells associated with sensory epithelium (col. 1, lines 58-64; col. 2, lines 1-27; col. 8, lines 24-27; claims 1-7). Carnahan also teaches that recombinant human NDFα2, and recombinant human NDFβ1 are effective in mitogenic stimulation of utricular sensory epithelial cells (column 9, lines 55-60; figure 5). The instant specification acknowledges that neu differentiation factor (NDF), which is the rat equivalent of human HRG (page 7, lines 39-40). Therefore, "human NDFα2" and "human NDFβ1" are synonymous with heregulin-α2, and heregulin-β1. Furthermore, the instant claims each recite variants and fragments of each recited species of heregulin. In the absence of a specific recitation of structural differences, all forms of heregulin are variants of one another. Therefore, Carnahan fully anticipates all of the growth factor, target cell, and intended use limitations of instant claims 1, 3-8, 10, 12, 14, and 16.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6017886 (Carnahan) as applied to claims 1-8, 10, 12, 14, and 16 above, and further in view of US Patent 5587458 (King *et al.*), issued December 24, 1996. Claim 9 is drawn to the method of claim 1 where wherein the HER2/3 activating ligand is an agonist antibody. As noted, Carnahan teaches the method of claim 1 wherein the HER2/3 activating ligand is a heregulin polypeptide. Carnahan does not, however, teach the use of an agonist antibody. King *et al.* teach (throughout) the construction and use of antibodies that bind and activate erbB2 (HER2) (see Abstract). Therefore, it would have been obvious to one of skill in the art at the time the invention was made to use an agonist antibody, such as taught by King *et al.*, in any protocol where activation of HER2/3 is desired, such as the stimulation of utricular sensory epithelial cells taught by Carnahan with a reasonable expectation of success.

12. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6017886 (Carnahan) as applied to claims 1-8, 10, 12, 14, and 16 above, and further in view of Carraway *et al.*, J. Biol. Chem. 269(19):14303-14306 (1994). Claim 11 recites

the recombinant human heregulin polypeptide, rHRG-β1-177-244, which is not specifically taught in the Carnahan patent. It was well known in the art at the time the instant application was filed that residues 177-244 of HRG-β1 comprise a fully functional growth factor domain. This is evidenced by Carraway *et al.*, who used this domain to demonstrate that erbB3 (HER3) is a receptor that mediates the activation of erbB2 (HER2) by heregulin (see abstract). Therefore, it would have been obvious to one of skill in the art to use rHRG-β1-177-244 in any protocol where activation of HER2/3 is desired, such as the stimulation of utricular sensory epithelial cells taught by Carnahan.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D.,whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647
17 July 2006

DAVID S. ROMEO
PRIMARY EXAMINER